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Comparison of procalcitonin, C-reactive protein, white blood cell counts and hemogram subparameters in community acquired pneumonia patients

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ABSTRACT

Aims: Pneumonia is a clinically and radiologically detected inflammation of the lungs. Most of the pneumonia patients are community-acquired pneumonia cases. Hemogram and C-reactive protein (CRP) are commonly used to support diagnosis and follow-up of treatment. Procalcitonin is less accessible and expensive. And the use of hemogram subparameters is not very common. The aim of this study was to research the relationship between procalcitonin, CRP, White Blood Cell count (WBC) and hemogram subparameters in patients with CAP and the efficacy of new hematologic rates in differential diagnosis.

Methods: Patients who were diagnosed with community acquired pneumonia by applying to the chest diseases outpatient clinic of our hospital were retrospectively analyzed. 67 patients who were clinically and radiologically diagnosed without noticing male or female were included in our study. Anamnesis data and co-morbidities of the cases were questioned. Procalcitonin, CRP and hemogram (platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR) were calculated and WBC value was examined) were recorded. The obtained data were evaluated statistically and compared in terms of variables.

Results: The mean age of our patients was 57 (18-71) years; there were 41 (61.19%) female and 26 (38.81%) male patients. 36 (53.73%) of our patients had chronic diseases; 21 (31.34%) had heart disease, 23 (34.32%) had diabetes, and 6 (8.95%) had kidney failure. Patients; 48 (71.64%) procalcitonin, 56 (83.58%) CRP, 38 (56.71%) WBC, 52 (77.61%) NLR, 34 (50.74%) PLR and 38 (56.71%) MLR values were high. Procalcitonin, CRP and NLR values were significantly higher than other subparameters. The CRP and NLR values of patients with an additional chronic disease were higher than patients without co-morbidities. In the correlation analyses, there was a strong correlation between procalcitonin, CRP and NRL, but the correlation between the others was not significant. ($p<0.001$).

Conclusion: Our study shows NLR from hemogram subparameters can be used safely in CAP patients. Procalcitonin is expensive test for. Considering that Procalcitonin is not available in primary care family health centers and CRP is found in some family health centers, the calculated use of NLR will support the diagnosis. Using fewer examinations in secondary and tertiary health facilities is also valuable in terms of reducing health costs.

Keywords: Pneumonia, NLR, procalsitonin, CRP

INTRODUCTION

Pneumonia is an inflammatory disease of the lung parenchyma caused by infectious agents (bacteria, viruses, parasites, fungi, etc.). It is a group of diseases with high mortality and morbidity in children and adults all over the world. Pneumonia that occurs during a person's daily life is called community-acquired pneumonia (CAP). It is stated that 5.6 million people are diagnosed with CAP annually in the United States of America (USA) and 1.1 million people require hospitalization due to CAP. CAP ranks sixth among all causes of death in the USA and first among deaths due to infections.[1,2] With age, the incidence increases. In a large-scale study in Germany, the overall incidence of CAP in adults over 18 years of age was 1,054 cases per 100,000 person-year observations. ≥18 adults, high mortality of hospitalized CAPs was observed in the hospital (18.5%) and after one year (44.5%). The mortality rate in older adults was more than doubled.[3] A large-scale research has been carried out in recent years by the Ministry of Health of the Republic of Turkey, the Directorate of Hygiene School of the Refik Saydam Sanitation Center and Başkent University. According to the final report announcing the results of the National Burden of Disease and Cost Effectiveness Project and published in December 2004; in the household survey,

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among the top 20 chronic and acute diseases diagnosed by a clinician in the last two months, pneumonias ranked 15th with a frequency of 1.15%.[4]

Pneumonia that occurs in individuals during their normal daily lives and in the community is defined as community-acquired pneumonia (CAP).[1,4] CAP is responsible for a significant proportion of doctor's consultation appointments, work-school day losses, treatment costs and disease-related deaths worldwide.[5,6] When the publications in our country covering pneumonia cases in the community are examined, it is seen that the rate of detecting the infectious agent varies between 21-62.8%.[7] Even if it is possible to determine the causative agent, empirical antibiotic treatment is required at least initially since culture and agent determination studies will require a certain amount of time.[8,9] Efforts are being made to prevent work-school power losses, reduce disease-related morbidities and reduce diagnosis and treatment costs are increasing. The reasons listed here have increased the need for the use of laboratory parameters in early diagnosis and prognosis by combining them with clinical findings. In recent studies, the role of many infectious markers in the diagnosis and prognosis of pneumonia has been investigated. The most commonly investigated include C-reactive protein (CRP), procalcitonin (PCT), platelet count, white blood cell (WBC) count, mean platelet volume (MPV) and interleukin-1.[10,11] C-RP is an elevated positive acute phase reactant in many infections and autoimmune diseases. Procalcitonin is a calcitonin precursor peptide that is absent or very low (<0.1 ng/ml) in healthy individuals and is increased in inflammatory and infectious conditions. In severe infectious conditions, sepsis and multiorgan failure, its synthesis is increased.[12]

Pneumonia severity index (PSI) and confusion, respiratory rate, blood pressure, 65 years and older (CURB-65), serum urea/creatinine values are commonly used tools among many scoring systems to assess disease severity and predict mortality in patients with CAP.[13] However, no scoring systems are ideal, and some scores are cumbersome to be used in everyday clinical practice. Inflammatory biomarkers such as blood-like CRP and procalcitonin may improve the prognostic accuracy of these scores.[14,15] However, these two biomarkers are not always reliable,[16] so the need to identify a reliable, inexpensive and easy-to-use biomarker arises. One of the markers studied involves the neutrophil-to-lymphocyte ratio (NLR), an easily measurable index. It is the ratio of the absolute number of neutrophils to the absolute number of lymphocytes. Under pathological stress, the number of neutrophils increases, while the number of lymphocytes decrease.

The aim of this study was to research the relationship between procalcitonin, CRP, white blood cell count (WBC), NLR and other hemogram subparameters in patients with CAP. The relationship was used to evaluate whether hemogram subparameters were as significant as CRP and procalcitonin in patients with community-acquired pneumonia.

METHODS

The study was carried out with the permission of Şişli Hamidiye Etfal Training and Research Hospital Clinical Researches Ethics Committee (Date: 02.05.2023, Decision No: 2316). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Due to the retrospective nature of the study, the need for written informed consent from patients was also waived.

Participants and Study Design

Between 10.10.2022 and 31.12.2022, patients diagnosed with CAP were admitted to the Chest Diseases Polyclinic of Health Sciences University Şişli Hamidiye Etfal Training and Research Hospital.

Patient records were examined retrospectively through the hospital computer data system. Patients with complete complaints, examinations and history file information, chest X-ray and/or computer tomography and laboratory tests were included in the study. Individuals over the age of 18, regardless of sex, were included in our study. Cases who had not been hospitalized for the last 15 days, who had not received antibiotic treatment in the last 15 days for any reason, who did not have known immune system disorders or malignancies, and who did not use steroids during the period of admission to our outpatient clinic were included in our study. Cases with missing files, immune system disorders and malignancies were not included in the study. The files and examinations of the patients were examined. Laboratory data of patients with confirmed diagnosis of pneumonia; procalcitonin, CRP and hemogram (neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR) were calculated and white blood cell (WBC) count value was examined) were uploaded to the excel program and the statistics were performed.

Statistical Analysis

For the Social Sciences (SPSS) for Windows 23.0 (IBM Corp., Armonk, NY) package program, patient data gathered within the scope of the study were assessed with the IBM Statistical Package .frequency and percentage values are given as frequency and percentage. Maximum, mean, and minimum descriptive values are given for continuous data. The normality test of the

data was performed by Kolmogorov-Smirnov Test. In the comparisons between the groups, "Independent Sample T-Test" was used for the two groups with normal distribution, "Mann Whitney-U Test" was used for those without normal distribution, and "Fisher's Exact Test or Chi-Square Test" was used for the comparison of categorical data items. Spearman's Correlation Examines was used to assess the relationship between laboratory measurements. The results were aforethought statistically remarkable when the p value was less than 0.05.

RESULTS

Between 10 September 2022 and 31 December 2022, patients diagnosed with CAP were admitted to the Chest Diseases Polyclinic of Şişli Hamidiye Etfal Training and Research Hospital, University of Health Sciences. Within four months of the study, 67 patients who were diagnosed with CAP clinically and radiologically who applied to the outpatient clinic were included without regard for sex. The median age of patients was 57.08±12.42 (18-71). A majority of the patients, 41 (61.19%) were female and 26 (38.81%) were male. The patient's body mass index (BMI) was 28.25±5.66 kg/m2. Additionally, 36 (53.73%) of our patients had chronic diseases; 21 (31.34%) had heart disease, 23 (34.32%) had diabetes and 6 (8.95%) had kidney failure. 23 (34.34%) of the patients were active smokers, 27 (40.29%) of them quit, and 17 (25.37%) of them had never smoked. Demographic data of the patients are demonstrated in Table 1.

Table 1. Baseline demographics of the study population

	Mean ± S.D.	Median (Min-Max)
Age	57.08±12.42	57 (18-71)
	n (67)	(%)
Gender		
Female	41	61,19
Male	26	38,81
Smoking		
Smoking	23	34,34
Quit	27	40,29
Never smoked	17	25,37
Chronic diseases		
Cardiac disease	21	31,34
Diabetes mellitus	23	34,32
Kidney failure	6	8,95
BMI	28.25±5.66	27.15 (17.28-49.7)

Cough was the most common complaint among the participants with 60 (89.55%) patients suffering from it. Chest pain was present in 46 (68.65%) patients, and sputum was in 52 (77.61%) patients. In addition, 41 (61.19%) patients had fever, 38 (56.71%) patients had shortness of breath, and 7 (10.44%) patients had hemoptysis.

The distribution of pneumonia was as follows: 29 (43.28%) had lobar pneumonia, 10 (14.92%) had multilobar pneumonia, and 28 (41.79%) had multisegmental nodular infiltration and interstitial changes.

The laboratory parameters were: glucose 144.97±51.32, alanine aminotransferase (ALT) 34.12±14.17, aspartate aminotransferase (AST) 43.01±26.27, urea 34.13±14.17, creatinine 0.37±0.21, lactic dehydrogenase 315±170, ferritin 393.57±351.84, hemoglobin 12.7±3.73, hematocrit 41.02±6.73. CRP was elevated in 56 (83.58%) patients, PCT in 48 (71.64%), WBC in 38 (56.71%), NLR in 52 (77.61%) patients, MLR in 38 (56.71%) patients, and PLR in 34 (50.74%) patients. The laboratory test results we used are demostrated in Table 2.

Table 2. Laboratory parameters of the study population

	Mean ± S.D.	Median (Min-Max)
WBC	9.79±4.73	8.32(3.38-19.88)
C-RP	84.67±48.70	77(1-303)
PCT	0.37±0.21	0.15(0.01-3.82)
NLR	7.90±4.27	5.38(1.11-55.67)
MLR	0.35±0.13	0.29 (0.20-0.51)
PLR	187±84	173 (92-573)

Laboratory data of CAP patients participating in our study were compared with correlation analysis. There was a low linear relationship between the NLR value and procalcitonin (r:0.454) value and a moderate linear relationship with the CRP (r:0.626) value of the patients. Similarly; There was also a moderate linear relationship between procalcitonin value and CRP values (r:0.595). There was no correlation between other hemogram subparameters and C-RP and procalcitonin. The results of the correlation analysis, in which the relationship between the laboratory measurements of the patients are evaluated, are given in Table 3.

Table 3. Evaluation of the relationship between NLR, procalcitonin and C-RP values

		NLR	PCT	C-RP
NLR	Correlation coefficient p-value	1.000 -	0.454 <0.001	0.626 <0.001
PCT	Correlation coefficient p-value	0.454 <0.001	1.000 -	0.595 <0.001
C-RP	Correlation coefficient p-value	0.626 <0.001	0.595 <0.001	1.000 -

DISCUSSION

Community acquired pneumonia (CAP) is responsible for the majority of admissions to hospitals, treatment expenses, lost work&school days and majority of deaths all around the world.[5,6] It's important to quickly diagnose the patient who has been admitted to the emergency department or to the polyclinic with complaints of

infection and to bring them into social life earlier. Studies on the usage of cheap and easily accessible blood biomarkers in the diagnostic phase of patients with CAP continue. In our study, we investigated the usability of hemogram sub parameters and especially NLR for this purpose. We found that NLR was as significant as other blood biomarkers such as PCT and CRP in diagnosis of CAP patients.

NLR is the ratio of the absolute neutrophil count to the absolute lymphocyte count. Under pathological stress, lymphocyte count decreases while neutrophil count increases. Early diagnosis and, accordingly, prompt treatment of patients with bacteremia, especially sepsis, are important as these improve prognosis. Initial stages of severe infection may be characterized by an increased number of neutrophils and fewer lymphocytes in the peripheric blood. Lowsby et al compared the neutrophil-lymphocyte ratio to conventional tests such as CRP and white cell count. According to the researchers NLR is not sufficient on its own to direct the clinical management of patients with suspected bacteremia even though it performs better than conventional infection markers. They reported that this has no advantage compared to WBC. Along with this, they stated that NLR was able to present some diagnostic benefits as a part of the general evaluation.[17] Jager et al.[18] described NLR as an indicator of bacteremia in medical emergencies. In their studies, they investigated the value of NLR in patients with CAP. They concluded that the NLR measured during an examination for pneumonia in the emergency department predicted the severity and outcome of CAP with a higher prognostic accuracy compared to conventional infection markers. In research conducted in Türkiye, Üçsular et al.[19] wrote that PLR and NLR were higher in all patients with hypersensitivity pneumonia compared to the control group and PLR and NLR, along with clinical, radiological and pathological findings, were cheap and simple parameters that may guide the diagnosis of hypersensitivity pneumonia and acute-chronic distinction of the illness. Şahin et al.[20] investigated the efficiency of WBC, CRP, PCT, NLR and PLR on diagnosis in patients, severity of the disease and response to treatment. They reported that PSI score of NLR showed significant correlation with leukocyte, neutrophil, lymphocyte, CRP, PCT and uric acid. Following the response to treatment they saw that leukocyte, NLR, CRP and PCT were rather beneficial, they reported that CRP and NLR which is especially cheaper and repeatable could be used more widely regarding PCR being more expensive compared to other measurements. We found that WBC, CRP, PCT, NLR and other hemogram sub parameters were high in our study. We detected WBC, CRP, PCT and NLR to be higher than other parameters.

More research is being conducted on NLR's ability to assist the diagnosis and prognosis of pulmonary infections observed in childhood age group and while being treated for nasocomial pneumonia. Omran et al.[21] reported that combined usage of lung ultrasound and NLR was beneficial for the differential diagnosis of viral/bacterial pneumonia in children. They proved that lung ultrasound was a noninvasive and reliable method for early diagnosis and differentiation of viral and bacterial pneumonia in little Egyptian children. The researchers evaluated this as "Combining NLR with lung ultrasound increased the diagnostic accuracy in evaluation of children suspected with pneumonia". Cheng et al.[22] retrospectively examined the patients hospitalized for acute stroke. They reported that NLR and serum fibrinogen may have greater negative diagnostic value in estimating stroke-related pneumonia in stroke patients, but combining NLR and serum fibrinogen can show an increasing value in predicting stroke-related pneumonia in patients with acute stroke. In a study NLR, CRP and PCT were compared to detect sepsis in 216 patients in intensive care and it was reported that NLR wasn't superior to other parameters.[23] In his study Zahorec defined NLR as a simple and quick parameter of systemic inflammation and stress in critically ill cases.[24] In two studies on COVID-19 correlation was observed between NLR and severity of the illness.[25,26]

In a study they conducted on 209 patients hospitalized for CAP, Curbelo et al.[27] reported that neutrophil levels and NLR are simple, cheap parameters with prognostic benefit, especially when measured in 3-5 days after CAP diagnosis. High NLR and/or neutrophil levels are associated with a higher risk of death in 90 days. In other studies, NLR is a simple, cheap and quick measurement in routine blood test and associated with adverse clinical outcomes in adult CAP patients.[28-30] In a review conducted on 3340 patients, NLR was featured as a simple, easily measured yet promising marker to estimate the outcomes in patients with CAP.[31] Meng et al.[32] couldn't find any connection between heparin-bound protein and CAP etiology but they showed that heparin-bound protein and NLR also increased with increasing severity as independent markers of 30-day death in CAP patients. Şahin et al.[20] saw that PCT widely used for the severity of diagnosis and treatment follow-up of patients with pneumonia was correlated with NLR and CRP. While they couldn't find any significant correlation between CURB-65 and PSI score with CRP, they saw a significant correlation between NLR and these scores. They concluded that WBC, NLR, CRP and PCT were rather beneficial for the follow-up of treatment response. In our study we found that NLR level was highly correlated with CRP ($p<0.01$). We found moderate correlation between NLR and PCT with WBC ($p<0.05$). There was no correlation between MLR and PLR with other values ($p>0.05$).

CONCLUSION

This study shows that NLR from hemogram subparameters can be used safely in patients diagnosed with community-acquired pneumonia. It should be borne in mind that procalcitonin is an expensive test. Considering that Procalcitonin is not available in primary care clinics and CRP is found in some of them, it has been shown that the use of NLR from hematological subparameters will support the diagnosis. Using fewer tests in secondary and tertiary health services also carries great value in terms of reducing health costs.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Şişli Hamidiye Etfal Training and Research Hospital Clinical Researches Ethics Committee (Date: 02.05.2023, Decision No: 2316).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients

Referee Evaluation Process: Externally peer-reviewed.

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